```
     (FILE 'HOME' ENTERED AT 17:26:39 ON 21 MAY 2001)

     FILE 'MEDLINE' ENTERED AT 17:26:45 ON 21 MAY 2001
L1        22797 S MULTIPLE (1W) SCLEROSIS
L2            0 S L1 AND (B (1W) CELL (1W) DEPLETION)
L3            5 S L1 AND CD20
L4            0 S NELSON MB/AU
L5          390 S NELSON M/AU
L6            0 S L5 AND CD20
L7            0 S L5 AND (B (1W) CELL (1W) DEPLETION)
L8         2632 S L1 AND ANTIBODY
L9            0 S L5 AND (B (1W) LYMPHOCYTE (1W) DEPLETION)
L10           0 S L1 AND (B (1W) LYMPHOCYTE (1W) DEPLETION)
L11           0 S L1 AND L5
L12         138 S L8 AND (B (1W) LYMPHOCYTE)
L13           5 S L12 AND DEPLETION
L14       24854 S L1 OR EAE
L15        3190 S L14 AND ANTIBODY
L16          81 S L15 AND DEPLET?
L17           0 S L14 AND RITUXIMAB
L18         198 S RITUXIMAB
L19         124 S L18 AND CD20
L20          67 S L18 AND CHIMERIC

     FILE 'REGISTRY' ENTERED AT 17:45:25 ON 21 MAY 2001

     FILE 'HOME' ENTERED AT 17:46:56 ON 21 MAY 2001

     FILE 'REGISTRY' ENTERED AT 17:49:39 ON 21 MAY 2001
L21           1 S RITUXIMAB

     FILE 'CAPLUS' ENTERED AT 17:52:03 ON 21 MAY 2001
L22          77 S L21
L23       12700 S L22 AND MS OR EAE OR SCLEROSIS
L24           1 S L22 AND (MS OR EAE OR SCLEROSIS)

     FILE 'BIOSIS' ENTERED AT 17:53:50 ON 21 MAY 2001
L25         253 S L21
L26           0 S L25 AND (MS OR EAE OR SCLEROSIS)

     FILE 'REGISTRY' ENTERED AT 17:54:22 ON 21 MAY 2001

     FILE 'DRUGPAT' ENTERED AT 17:55:01 ON 21 MAY 2001
L27          37 S L21
L28           0 S L21 AND (MS OR EAE OR SCLEROSIS)

     FILE 'MEDLINE' ENTERED AT 17:55:36 ON 21 MAY 2001
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L3 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 92147284 MEDLINE
DOCUMENT NUMBER: 92147284 PubMed ID: 1783458
TITLE: Preferential reductions in lymphocyte sub-populations induced by monthly pulses of chlorambucil: studies in patients with chronic progressive **multiple sclerosis**.
AUTHOR: Chiappelli F; Myers L W; Ellison G W; Liao D; Fahey J L
CORPORATE SOURCE: Psychoneuroimmunology Program, University of California, Los Angeles 90024.
CONTRACT NUMBER: AI 07126 (NIAID)
AI 15332 (NIAID)
SOURCE: INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1991) 13 (5) 455-61.
Journal code: GRI; 7904799. ISSN: 0192-0561.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920317

AB Thirty-three patients with chronic progressive **multiple sclerosis** (MS) were assigned to intervention groups receiving monthly pulses of chlorambucil (CB) for about one year. The monthly doses ranged from 0.4 to 1.5 mg/kg. Administration of CB resulted in preferential reduction in different lymphocyte subsets which was dose- and time-dependent. The number of B-cells (**CD20**) decreased more rapidly than NK-cells (CD16, CD56, CD16+CD56+) or T-cell (CD3) and T-cells subsets (CD4 and CD8). At 1.2 mg/kg, CB administration resulted in a preferential drop of T-suppressor/cytotoxic cells (CD8) compared with T-helper cells (CD4), and of the less mature "virgin" CD4 cells (CD4+CD45RA+) compared with "memory" CD4 cells (CD4+CD45RA-). The expression of activation markers (transferrin receptor, CALLa, HLA-Dr and CD38[OKT10]) within CD4, CD8 or **CD20** lymphocytes was not altered by CB administration. Our data, which show that CB administration results in a preferential fall in B-cell numbers, contrast with the effects of long-term administration of the related immunosuppressive drugs, azathioprine and cyclophosphamide.

L20 ANSWER 4 OF 67 MEDLINE
ACCESSION NUMBER: 2001194878 MEDLINE
DOCUMENT NUMBER: 21117639 PubMed ID: 11226006
TITLE: **Rituximab**: an insider's historical perspective.
AUTHOR: Grillo-Lopez A J
CORPORATE SOURCE: Medical and Regulatory Affairs Division, IDEC Pharmaceuticals Corporation, San Diego, CA 92121, USA.
SOURCE: SEMINARS IN ONCOLOGY, (2000 Dec) 27 (6 Suppl 12) 9-16. Journal code: UN5; 0420432. ISSN: 0093-7754.
PUB. COUNTRY: United States
Historical
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered PubMed: 20010227
Entered Medline: 20010405

AB **Rituximab** (Rituxan; Genentech, Inc, South San Francisco, CA and IDEC Pharmaceutical Corporation, San Diego, CA) is a unique monoclonal antibody for the treatment of non-Hodgkin's lymphoma. This **chimeric** mouse/human antibody was discovered in 1991 at IDEC Pharmaceuticals' laboratories, where the antibody was genetically engineered and produced utilizing high-yield expression systems. It is a human IgG1 kappa antibody with mouse variable regions isolated from a murine anti-CD20 antibody, IDEC-2B8, that binds with high affinity to cells expressing the CD20 antigen found on the surface of malignant and normal B cells, but not on other normal tissues. It mediates complement-dependent cell lysis in the presence of human complement, and antibody-dependent cellular cytotoxicity with human effector cells. Also, it has been shown to induce apoptosis and to sensitize chemoresistant human lymphoma cell lines in vitro. Clinical development was expedited (3 years) with the first patient entered in phase I trials in March 1993 and the last patient entered in the phase III study in March 1996. IDEC Pharmaceuticals began a collaboration with Genentech, Inc in March 1995 and with F. Hoffman-LaRoche (Nutley, NJ) shortly thereafter. Marketing approval was granted by the US Food and Drug Administration on November 26, 1997 (and by the European Union on June 2, 1998) for the indication of relapsed or refractory, CD20-positive, B-cell, low-grade or follicular non-Hodgkin's lymphoma. **Rituximab** is the first therapeutic monoclonal antibody approved for the treatment of cancer and the first single agent approved specifically for therapy for a lymphoma. Substantial research has been performed over the past 8 years to further the understanding of this novel therapeutic. Nevertheless, much remains to be accomplished in key areas such as mechanism of action and resistance, combinations with chemotherapy, biologics and radiotherapy/radioimmunotherapy, role within multimodality regimens, and nonmalignant applications. Research conducted in the coming years should be targeted toward resolving these important issues.

L24 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:814347 CAPLUS
DOCUMENT NUMBER: 133:361915
TITLE: Treatment of autoimmune diseases with antagonists which bind to B cell surface markers
INVENTOR(S): Curd, John G.; Kunkel, Lori A.; Grillo-Lopez, Antonio J.
PATENT ASSIGNEE(S): Genentech, Inc., USA; Idec Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067796	A1	20001116	WO 2000-US40018	20000504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-133018 P 19990507
US 1999-139621 P 19990617

AB The present invention concerns treatment of autoimmune diseases with antagonists, e.g. antibodies, which bind to B cell surface markers, such as CD19 or CD20.

REFERENCE COUNT: 5
REFERENCE(S):
(1) Johnston, P; BLOOD, PART 2 1999, V94(10, SUPP 1), P4386
(2) Lee, E; BLOOD 1998, V92(9), P3490 CAPLUS
(3) Mow, B; BLOOD, PART 2 1999, V94(10, SUPP 1), P3526
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(5) Univ Leland Stanford Junior; WO 9503770 A 1995 CAPLUS

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#9	Link to **PubMed** from (**11332657**)	07:32:32	101
#1	Search **multiple sclerosis review**	07:30:23	3076

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1: Clegg A, Bryant J. Relate

Immunomodulatory drugs for multiple sclerosis: a systematic review of clinical and cos effectiveness.
Expert Opin Pharmacother. 2001 Apr;2(4):623-39.
PMID: 11336612 [PubMed - in process]

2: O'Connor KC, Bar-Or A, Hafler DA. Relate

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J Clin Immunol. 2001 Mar;21(2):81-92.
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Identification of autoantibodies associated with myelin damage in multiple sclerosis.
Nat Med. 1999 Feb;5(2):170-5.
PMID: 9930864 [PubMed - indexed for MEDLINE]

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